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Resolution After Radiotherapy Of Severe Pulmonary Damage Due To Paraquat Poisoning

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Source: *British Medical Journal (Clinical Research Edition)*, Vol. 288, No. 6426 (Apr. 28, 1984), pp. 1259-1260

Published by: [BMJ Publishing Group](#)

Stable URL: <http://www.jstor.org/stable/29514924>

Accessed: 19/07/2013 06:50

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Experiments in animals show that embolisation of the hepatic artery with relatively large particles of absorbable gelatin sponge results in less derangement of liver function and less risk of hepatic failure or abscess than embolisation of the more peripheral hepatic tree with silicone cement.⁴ Embolisation of small vessels, however, is more effective in delaying the formation of a collateral circulation. Our technique used combinations of absorbable gelatin sponge, human thrombin, and Lyodura. Absorbable gelatin sponge and strips of Lyodura approximately 1×10 mm were used as the initial embolising materials, and human thrombin was added when satisfactory occlusion had not been achieved. Thus our technique may have resulted in relatively proximal arterial occlusion and spared the terminal arteries and arterioles.

Portal venous obstruction is an absolute contraindication to hepatic arterial embolisation and hepatic cirrhosis a relative contraindication; in cirrhosis the liver parenchyma is more dependent on the hepatic arterial supply than normal. Nevertheless, two of the three patients we treated who had cirrhosis survived longer than 28 days; one woman aged 47 died at 11 months, and another woman aged 28 was still alive at three months when she returned to her own country and was lost to follow up.

Jaundice has also been suggested as a relative contraindication to hepatic dearterialisation,⁵ though this has been disputed.⁶ Only five of our patients had serum bilirubin concentrations within the normal range (two in group 1, three in group 2), and we did not find the serum bilirubin concentration useful in predicting outcome in this high risk group of patients. Tumours may produce localised intrahepatic biliary obstruction,⁷ and embolisation experiments in monkeys⁸ show an increased risk of abscess formation in areas of liver whose biliary outflow is obstructed. Local biliary obstruction may explain the predictive value of the raised serum alkaline phosphatase activity. The

preponderance of pancreatic tumours in group 1 is noteworthy.

Our findings suggest that a weighted combination of serum alkaline phosphatase activity and serum albumin concentration may be used to predict a subgroup of patients with extensive hepatic tumours who can be treated with hepatic arterial embolisation. Our findings could be readily tested in other series retrospectively before clinical application and, if confirmed, would permit safe single palliative embolisation of large painful tumours.

We thank Dr K D Macrae, of the department of medical statistics, for help with the discriminant analysis and Mrs Christine Smith for typing the manuscript.

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(Accepted 3 February 1984)

Resolution after radiotherapy of severe pulmonary damage due to paraquat poisoning

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Abstract

A 29 year old man was admitted 36 hours after ingesting about 5 g paraquat. His arterial oxygen pressure fell progressively to 3.4 kPa (34 mm Hg), and pulmonary damage induced by paraquat was diagnosed. His condition did not improve after treatment with prednisolone and cyclophosphamide, but after irradiation both lungs cleared and arterial oxygen pressure started to improve.

Irradiation of the lungs should be considered in patients

who, after surviving the acute phase of poisoning with paraquat, show progressive deterioration of respiratory function.

Introduction

Pulmonary disease induced by paraquat has an almost uniformly fatal outcome. We describe a patient in whom the pressure of arterial oxygen fell to 4.6 kPa (34 mm Hg) despite treatment with a combination of cyclophosphamide and prednisolone but whose condition improved after radiotherapy to the lungs.

Case report

A 29 year old man was admitted to hospital because he said that he had taken some Weedol a few hours earlier. Urine screening by the alkaline dithionate method confirmed the presence of paraquat. After undergoing stomach washout he was treated with fuller's earth. Charcoal haemoperfusion was started but was stopped when the serum paraquat concentration on admission was found to have been only 429 $\mu\text{mol/l}$ (80 mg/l). He later admitted that he had taken two packets of Weedol (5 g paraquat) 36 hours before coming to hospital.

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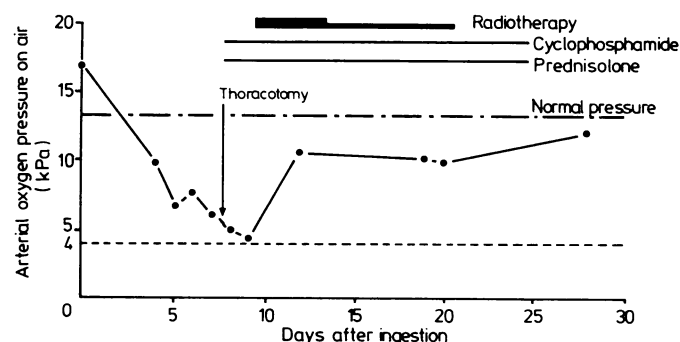
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On admission a chest radiograph and urea and electrolyte concentrations were normal and his arterial oxygen pressure was 17.3 kPa (127 mm Hg) during overbreathing. By day 3, however, his creatinine clearance had fallen to 37 ml/min, and on day 4 he complained of dyspnoea. Chest x ray examination showed patchy bilateral pulmonary shadowing, which was most pronounced in the mid and lower zones and worsened in parallel with the fall in arterial oxygen pressure that occurred (figure). Because of the inconsistent history and the doubt about the dose of paraquat and the time at which it had been taken a limited left thoracotomy and lung biopsy were done on day 8. The biopsy specimen contained paraquat (0.28 µg/g) and showed diffuse alveolar damage and cellular proliferation with numerous alveolar macrophages and some hyaline membranes, consistent with the diagnosis of pulmonary damage due to paraquat.



Arterial oxygen pressure and treatment received after ingestion of paraquat.

Cyclophosphamide 3 mg/kg body weight and prednisolone 1 mg/kg were started, but the arterial oxygen pressure continued to fall for a further 36 hours. Radiotherapy was started: both lungs were irradiated with parallel opposed fields of γ rays labelled with cobalt-60. The right lung received 11.25 Gy (1125 rad) (five fractions over four days) and the left 15.0 Gy (1500 rad) (10 fractions over 11 days), both doses uncorrected for increased transmission through the lung. Pulmonary opacification improved, the right lung clearing more rapidly than the left. There was a rapid and sustained improvement in arterial oxygen pressure.

Nine months later arterial oxygen pressure showed no further change, transfer factor remained half the predicted value, and the patient was asymptomatic apart from developing dyspnoea on exertion. There were no physical signs, and a chest radiograph was normal apart from showing non-absorbable suture material.

Discussion

Paraquat is a compound with a high electron affinity: its toxicity is related to exhaustion of intracellular nicotinamide adenine dinucleotide phosphate ions and generation of oxygen free radicals. Histological studies in animals have shown an early phase of alveolar destruction followed some days later by infiltration of rapidly dividing cells, which mature and lay down collagen, producing fatal fibrosis.¹ Extensive alveolar damage has been observed in people who have died after taking large doses of paraquat.² After lower doses, as in the present case, lung damage of insidious onset is associated with intra-alveolar fibrosis.²⁻³ The paraquat concentration of 429 µmol/l (80 mg/l) seen in our patient 36 hours after ingestion was consistent with such an outcome.⁴ Spontaneous recovery has been described in some patients with clinical and radiological evidence of lung damage, and treatment with prednisolone and cytotoxic drugs has been advocated in an attempt to interfere with the proliferation of fibroblasts.³⁻⁵ Few reports of spontaneous recovery, however, have included full details of serum paraquat concentrations or serial function studies.

Our patient was seriously affected and was on the point of requiring ventilation. His condition had deteriorated after conventional treatment, and death appeared to be inevitable. Fibroblasts are radiosensitive in vitro, and low doses of irradiation

can prevent the proliferation of fibroblasts that leads to formation of keloid. Both lungs were therefore irradiated, which produced a rapid response (figure). Radiography showed that the right lung, which received the shorter but more intensive course of treatment, improved faster than the left. This assessment was complicated by the effects of the biopsy of the left lung but suggests that the improvement was a result of the irradiation rather than a delayed effect of the drug treatment.

The doses of x rays were chosen to be well below lung tolerance because the patient was taking concurrent cytotoxic drugs, his lungs were already damaged, and paraquat is a radiosensitiser that persists in lung tissue. Nine months later there was no evidence of delayed deterioration in lung function, although late onset radiation fibrosis was still possible.

In the management of poisoning with paraquat, paraquat concentrations provide prognostic information.⁴ In those patients who survive the acute phase but are at any risk of damage to the lungs serial chest radiographs, blood gas tensions, and lung function (unless oral ulceration prevents this) should be monitored. If progressive deterioration of respiratory function develops low dose irradiation of the whole of both lungs should be considered. Careful monitoring should allow successful treatment to be differentiated from spontaneous recovery.

We thank Dr G A Coles for permission to report this case and Dr Lewis Smith, Central Toxicology Laboratory, Imperial Chemical Industries, Alderley Edge, Cheshire, for analysis of paraquat in the lung.

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(Accepted 8 February 1984)

ONE HUNDRED YEARS AGO We understand that the Special Purposes Sanitary Committee of the Metropolitan Board of Works has recommended that the Board should urge on the Home Secretary the desirability of the amendment of the Infant Life Protection Act, with a view of making the registration of every person receiving one child to nurse compulsory, and to provide for proper inspection. It was stated at the Board that representations had been several times made to the Home Office on this subject. In the meantime, and just as the clerk at the Home Office pigeon-holes the letter, we are again startled by a most shocking and inhuman case of the starvation of several children, and the deaths of two of them, who had been received by a single woman to nurse in answer to advertisements. The money received by her from the parents was spent in drink, the infants being kept for days without food. She was arrested in a public house, taken before the magistrate at Milton Courthouse, and remanded, crying out as she left the dock, "All right, do what you like with me." It ought to be impossible for a drunken ogre to have it in her power to cause dreadful human suffering to little children, nearly all of whom were under three years of age. Such children are quite helpless; they cannot tell their tale of suffering to the neighbours or to the police, neither can they run away, as older children would. They should all, up to the age of three years, be brought under the provisions of the Infant Life Protection Act, as was in the first instance proposed by the Infant Life Protection Society. (*British Medical Journal* 1884;ii:180.)